8-22-99

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DATA EVALUATION RECORD

PROHEXADIONE CALCIUM TECHNICAL
(BX-112)

Study Type: §81-2; Acute Dermal Toxicity

Work Assignment No. 1-02-25II (MRID 44457743)

Prepared for
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Disclaimer

This Data Evaluation Record may have been altered by the Health Effects Division subsequent to signing by Dynamac Corporation personnel.

For NK Mizpah 8/22/99

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For SD Mizpah 8/22/99

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rat
OPPTS Number:, 870.1200 OPP Guideline Number: §81-2

DP BARCODE: D246707 SUBMISSION CODE: S543930
P.C. CODE: 112600 TOX. CHEM. NO.: None

TEST MATERIAL (PURITY): Prohexadione calcium technical (92.1% purity)

SYNONYMS: BX-112; calcium salt of 3,5-dioxo-4-propionylcyclohexane-1-carboxylic acid; KIM-112; KUH-833

CITATION: Yamamoto, T. (1988) BX-112 technical: acute percutaneous toxicity study in rats. Biosafety Research Center, An-Pyo Center, Shizouka-ken, Japan. Laboratory Report Number 1070/1249. September 5, 1988. MRID 44457743. Unpublished.

SPONSOR: BASF Corporation, P.O. Box 13528, Research Triangle Park, NC.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44457743), five young adult F344 (SPF) rats/sex were dermally exposed to prohexadione calcium technical (92.1% purity) at 2,000 mg/kg (limit dose) for 24 hours. The test substance was mixed with 1 mL distilled water per animal and applied to approximately 10% of the total body surface area. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >2,000 mg/kg (observed)
Females = >2,000 mg/kg (observed)

Prohexadione calcium technical is classified as **TOXICITY CATEGORY III** based on the observed LD_{50} values for both sexes.

All animals survived and appeared normal during the 14-day observation period. No dermal irritation was reported. No significant treatment-related effect on body weight was observed in males. Although one female lost weight between 0 and 7 days, her overall weight gain was comparable to the remaining females by 14 days. Necropsy after 14 days revealed no observable abnormalities.

This study is classified **acceptable (§81-2)** and satisfies the guideline requirement for an acute dermal study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Prohexadione calcium technical (BX-112)
   Description: White-pale yellow powder
   Lot/Batch #: G14-03
   Purity: 92.1%
   CAS #: 127277-53-6

2. Vehicle: 1 mL distilled water per application

3. Test animals: Species: Rat
   Strain: F344 (SPF)
   Age: Young adult (8 weeks)
   Weight: 195-200 g males; 132-136 g females
   Source: Charles River Japan Inc., Shimofurusawa 795, Atsugi-shi, Kanagawa-ken, Japan
   Acclimation period: 9 Days
   Diet: Commercial rat and mouse diet MF (Oriental Yeast Co., Ltd., Kodenma-cho 10-11, Nihonbashi, Chuo-ku, Tokyo), ad libitum
   Water: Tap water, ad libitum
   Housing: Five animals/cage (by sex) in wire mesh cages
   Environmental conditions:
   Temperature: 22-24 °C
   Relative humidity: 50-60%
   Air changes: 20/Hour
   Light: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: July 27 - August 10, 1988

2. Animal assignment and treatment: Fur from the dorsal trunk area (6 x 7 cm) of five young adult F344 (SPF) rats/sex was clipped approximately 24 hours prior to dermal

administration of prohexadione calcium technical at 2,000 mg/kg (limit dose). To enhance dermal contact, the test material was mixed with 1 mL distilled water per treatment and uniformly applied to the clipped skin. The actual size of the application area was not specified; however, the clipped site (42 cm^2) is equivalent to approximately 14-18% of the total body surface area of a 135-200 g rat. Each test site was covered with a gauze patch, aluminum film, and surgical tape. After 24 hours, the coverings were removed, and the application sites were washed with distilled water. The rats were observed for signs of gross toxicity and/or mortality once each hour for 8 hours following application, and at least twice daily thereafter for up to 14 days. It was not specified if dermal irritation was observed and/or graded. Body weights were recorded at 0 (prior to dosing), 7, and 14 days. At 14 days, the surviving animals were sacrificed, necropsied, and examined for gross pathological changes.

3. Statistics: Not applicable to this study.

II. RESULTS AND DISCUSSION:

A. Mortality: All animals survived the 14-day observation period.

Dermal LD_{50} Males = >2,000 mg/kg (observed)
Females = >2,000 mg/kg (observed)

B. Clinical observations: No signs of toxicity were observed. No dermal irritation was reported.

C. Body Weight: No significant treatment-related effect on body weight was observed in male animals, who exhibited an overall (0-14 days) average increase of 19%. The body weight of one female decreased slightly between 0 and 7 days, then recovered by 14 days. All females exhibited overall gains, ranging from 11-19%.

D. Necropsy: Necropsy after 14 days revealed no observable abnormalities.

E. Deficiencies: The actual size of the application area was not specified. Since the clipped area encompassed approximately 14-18% of the total body surface area for 135-200 g rats, it is likely that at least 10% of the surface area was treated. In addition, it is evident from the results of this study as well as those obtained from a concurrently-submitted acute dermal toxicity study (MRID 44457737) conducted with prohexadione calcium (74.9% purity), that the test material is of low toxicity via the acute dermal route, and therefore this deficiency is considered minor.

EPA recommends that rats used for acute toxicity studies weigh at least 150 g. In this study, females weighed between 132 and 136 g at study initiation. This deficiency is

considered minor, however, and should have no effect on the results of the study.